

Prasugrel is an <u>ADP</u> receptor antagonist currently being developed by Sankyo Pharmaceuticals while produced by Ube Pharmaceuticals. Prasugrel is currently under (US) clinical development in cooperation with Eli Lilly Pharmaceuticals. It is designed to be used in conjunction with PCI (percutaneous coronary intervention.)



# Important information regarding percutaneous coronary intervention procedures;

"...Invasive diagnosis procedures for heart disease also have many side effects, including the possibility of scratching your arteries, which may accelerate the formation of both vulnerable and calcified plaque. A very popular but highly invasive conventional diagnostic procedure is cardiac catherization, popularly known as an angiogram. Typically, a cardiologist will recommend an angiogram when a patient "fails" an exercise stress test. The procedure consists of inserting a catheter (a long tube) into a large vein (usually in the leg) and threading it to the heart. A dye is injected and X-ray images are taken. Blockages can be diagnosed by changes in the rate of flow of the dye near occluded portions of the coronary arteries.

The invasive nature of the procedure creates significant risks: it may actually cause heart attacks, heart arrythmias, and infection. (79) There is also a risk of damaging the sensitive lining of the coronary arteries, thereby encouraging the formation of new vulnerable plaque.

We strongly recommend that patients avail themselves of the growing arsenal of noninvasive diagnostic procedures that can accomplish as much as or more than conventional angiography. Once fully developed, the new non-invasive UF CT heart scans and MRI scans, which can image vulnerable plaque, will be even more informative, particularly since angiograms are unable to detect vulnerable plaque. At the beginning of this chapter, we discussed how the two most popular forms of conventional invasive treatment for heart disease (coronary bypass surgery and balloon angioplasty) fail to address the true cause of heart disease, which is vulnerable plaque.

The number of these procedures used with patients is excessive, even by published medical standards. Many studies show little or no difference in outcomes between groups of patients treated with statin drugs versus surgery. (80) while other studies question the appropriate application of these surgeries. (81) We believe that the vast majority (at least 90 percent) of bypass surgeries could be avoided and that patients would achieve more effective reversal of coronary plaque, both vulnerable and calcified, through the noninvasive means described in this book. In general, bypass surgery is a palliative (pain suppressant) to reduce angina pain, although even this symptom can quickly be reduced through noninvasive means in most cases. There's a small number of cases in which the coronary arteries are so blocked that a heart attack may occur without the eruption of vulnerable plaque. For them, we do recommend bypass surgery or angioplasty. However, only a small percentage of bypass surgeries performed actually fall into this category. (82)

Bypass surgery is extremely invasive and involves actually stopping the patient's heart during the surgery. A heart-lung machine sustains the patient's life functions during this time. Many of the complications arise from the process of stopping the heart, the use of the heart-lung machine, and the difficult and uncertain process of restarting the heart.

Cognitive Decline from Surgery

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[One of the more disturbing issues in the use of conventional, invasive therapies is the likelihood of a significant decline in mental function and mood, including cognitive decline, depression, and mood swings. Some physicians have dismissed this concern as a temporary phenomenon, but studies have found the decline to be permanent for approximately half of all bypass patients. A study reported in the New England Journal of Medicine that followed 261 bypass patients over five years found significant and lasting decline in mental status.(83) Measures of intellectual function declined by an average of 36 percent at 6 weeks after surgery and 24 percent at six months; 41 percent of the patients had significant cognitive decline five years after bypass surgery. The researchers concluded that cognitive decline immediately after bypass surgery (which is widespread) was significantly associated with continued decline five years later.]

There are many risks and complications associated with bypass surgery. We mentioned above the 2 to 6 percent chance of dying from the surgery itself. In addition, there are risks of a nonfatal heart attack, stroke, nerve damage, and prolonged recovery periods.

As we reported at the beginning of this chapter, balloon angioplasty surgery may be effective in temporarily reducing angina pain, but studies have not reported significant reductions in subsequent heart attacks or deaths. Angioplasty compresses calcified plaque but does not address the basic process that creates vulnerable plaque, the true cause of most heart attacks. In fact, this invasive surgery has a high potential to irritate a region of calcified plaque, causing it to become unstable, therby encouraging inflammation and vulnerable plaque formation. It also has the potential to damage the delicate lining of coronary arteries, which also encourages the formation of soft plaque.

The use of stents, which has become a standard refinement since 2000, has not appreciably changes these outcomes. Another innovation developed by Johnson & Johnson is to coat the stents with a drug called sirolimus, which discourages cell growth and thereby significantly reduces restenosis, the tendency of cell growth in and around the stent, causing it to close up after surgery.(84) We expect that this form of angioplasty will become dominant because of the substantially improved restenosis rate. However, this improved form of angioplasty still addresses only areas of occlusion (blockage) from calcified plaque, so it misses the real danger: the more widely distributed regions of vulnerable plaque, which are far more likely to rupture and trigger a heart attack. All of the other dangers of damaging blood vessels and encouraging inflammation from this invasinve procedure remain unaffected by this refinement.

The invasive forms of treatment tend to be crude palliatives with many serious complications and risks and with little if any improvement in outcomes. The great advantage of the noninvasive means of stopping and reversing both vulnerable and calcified plaque is that they truly heal the source of the problem. With sufficient diligence and attention, almost everyone can avoid heart disease, invasive treatments, and the enormous suffering and death toll that this disease creates."

from - "Fantastic Voyage" by Ray Kurzweil and Terry Grossman, MD - pages: 228-231

#### Resources

\* External Counterpulsation to treat angina \*

Anti-platelet agents (American Heart Association)

Acute Coronary Syndrome (American Heart Association)

NLM (Pubmed) search results for 'prasugrel', 'LY640315', and 'CS-747'

Clinicaltrials.gov search results for 'prasugrel', 'LY640315', and 'CS-747'

Sankyo Pharmaceuticals - 'CS-747' (prasugrel)

Eli Lilly Pharmaceutical Corporation - 'LY640315' (prasugrel)

### Google search results - "eli lilly" +truth

## Big Pharmaceutical Companies - caveat emptor!

Percutaneous intervention is big business - make sure you really need it and understand the risks. 20th century technology provides us with a wealth of non-invasive means to increase your cardiovascular health - consult your physician and seek the opinions of the brightest minds while also researching the options for yourself.

#### References

(79) "Angiogram: what risks are there from the test?" *Harvard Medical School Family Health Guide* 

(www.health.harvard.edu/fhg/diagnostics/angiogram/angiogramRisks.shtml.)

(80) "No significant differences in outcome were noted between: Veterans treated medically and surgically (R.J. Scott et al. 1987. "Comparison of medical and surgical treatment for unstable angina pectoris." *N Engl J Med.* Apr 16;316(16): 977-984).

Hospitalized patients in Sweden receiving dramatically less surgical intervention than in the U.S. (P. G. McGovern et al. 1997. "Comparison of medical care and one and 12-month mortality of hospitalized patients with acute myocardial infarction." *Am J Cardiol*. Sept 1;80(5): 557-562).

Patients in different parts of the U.S. receiving radically different types of care (L. Pilote et al. 1995. "Regional variation across the United States in the management of acute myocardial infarction." *N Engl J Med.* Aug 31;333(9): 589-590).

At the same time, significant differences in outcome have been associated with better oversight of patients and lifestyle changes. Note, however, that the selection of patients can influence the results from comparative studies. Studies that screen out sicker patients will inevitably show fewer differences between surgical and medical treatment.

(81) C. M. Winslow et al. 1988. "The appropriateness of performing coronary artery bypass surgery." JAMA. Jul 22-29;260(4): 505-509; R. Lange and D. L. Hillis. "Use and overuse of angiography and revascularization for acute coronary syndromes." N Engl J Med. 338(25): 1838-1839.

While the health care system in the United States is set up to encourage the overuse of expensive treatments, patients and patient's families play their part as well by assuming that more expensive options are necessarily better.

(82) S. G. Ellis et al. 1992. "Randomized trial of late angioplasty versus conservative management for patients with residual stenosis after thrombolytic treatment of myocardial infarction." *Circulation*. Nov;86(5): 1400-1406. This study "strongly suggests" patients who had an "uncomplicated myocardial infarction" should be treated medically (with

drugs) rather than through surgery.

Another study concluded, "because conservative strategy achieves equally good short and long term outcomes with less morbidity and a lower use of [angioplasty], it seems to be the preferred initial management strategy." W. J. Rogers et al. "Comparison of immediate invasive, delayed invasive, and conservative strategies after tissue-type plasminogen activator." *Circulation*. May;81(5): 1457-1476. For the guidelines the medical profession uses to grade the seriousness of occluded arteries, see the report from the American College of Cardiology Foundation and American Heart Association, "ACC/AHA 2002 Guideline Update for the Management of Patients with Chronic Stable Angina."

E. Schneider et al. 2001. "Overuse of coronary artery bypass graft surgery and percutaneous transluminal coronary angioplasty." *Annals of Internal Medicine*. Sept 4;135 (5): 328-337; W. E. Boden et al. 1998. "Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy." N Engl J Med. 338: 1785; E. Braunwald. 1988. "Evolution of the management of acute myocardial infarcation: a 20th-century saga." *Lancet*. 352: 1771-1774.

The following articles speak to the "sickest subset" issue: <a href="https://www.clevelandclinic.org/heartcenter/pub/news/archive/2004/survival4\_29.asp">www.clevelandclinic.org/heartcenter/pub/news/archive/2004/survival4\_29.asp</a> and <a href="https://www.dukemednews.org/news/article.php?id=6479">www.dukemednews.org/news/article.php?id=6479</a> (See also notes on 6 and 7 on page 412.)

- (83) M. F. Newman et al. 2001. "Longitudinal assessment of neurocognitive function after coronary artery bypass surgery." N Engl J Med. Feb 8;344(6): 395-402.
- (84) "No development in interventional cardiology has created a stir like the drug-eluting stent for preventing restenosis.... Finally, in our excitement about the potential for interventional cardiology, we must remember that atherosclerosis will not be cured by drug-eluting stents. Prevention of progression of this disease requires changing the metabolic milieu of the patient who has it. Interventional procedures are superb for alleviating the current ischemia and related symptoms, but a concerted effort by the healthcare team and the patient are necessary to change the ultimate outcome. Although the restenosis mouse 'has roared,' it may not be necessary in all cases to use an elephant gun to eliminate him." S. King. "Restenosis: the mouse that roared." *Circulation*. 108: 248.

In addition, "sirolimus-eluting stent edge restenosis is frequently associated with local trauma outside the stent." P.A. Lemos et al. "Coronary restenosis after sirolimus-eluting stent implantation: morphological description and mechanistic analysis from a consecutive series of cases." *Circulation*. Jul 22:108(3): 256-260.

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